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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,243	01/04/2002	Paul I. Freimuth	BSA 01-22	6646

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EXAMINER	
GUIDRY, GUY L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,243	FREIMUTH ET AL.	
	Examiner	Art Unit	
	Guy Guidry, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53,63,64 and 87-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53, 63, 64, 87-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *pages 2&3, 7/1/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response filed on 9 February 2006 to the Non-Final Office Action mailed 9 August 2005 is acknowledged. Claims 53, 63, 64, 87, 89, 90, 91 and 93 have been amended. Claims 54-62 have been cancelled. New claims 94-98 have been entered. Claims 53, 63, 64, 87-98 are pending and under consideration in this Action.

Claim Objections

Claims 63, 88, 89 and 91 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are drawn to vectors wherein the amino acids encoded by the peptide extension in the independent claims from which the claims depend may be substituted to any other to any other amino acid residue. Therefore, the dependent claims are generic to the species peptide extension sequences in claims 53 (claim 63), 87 (claims 88 and 89) and 90 (claim 91).

Claim Rejections - 35 USC § 112

Response to Applicants' amendments and arguments

Claims 54-60 have been cancelled rendering all rejections under *35 USC § 112* to these claims moot.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53, 63, 87-91, 94-96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 is drawn to a peptide extension which comprises the carboxy-terminal 57 amino acid residues of the T7 gene 10B protein. Dependent claim 63 is drawn to any peptide of any sequence resulting from amino acid substitutions of the encoded peptide extension of claim 53, as long as the substitutions result in a net negative charge of between –2 to –20. Thus dependent claim 63 embraces *any* peptide sequence that is equivalent in length to the peptide extension sequence of claim 53 that is within the boundaries of the net negative charge restriction. This suggests that the T7 gene 10B protein sequence in claim 53 may be replaced by an entirely different sequence, which is not specified. This indefiniteness has 2 repercussions for claim interpretation.

1. Claim 53 may be considered indefinite for failing to particularly point out and distinctly claim the subject matter of the invention, the extension being variable and undefined, and dependent claims 63, 87-89, 94 also indefinite for depending from an indefinite claim.

2. Claim 53 may be considered indefinite and dependent claims 63, 87-89 and 94 further indefinite for having insufficient antecedent basis for limitations in the claims. If any or all of the amino acid residues of the peptide extension of independent claim 53 may be substituted, then 53 is also indefinite with respect to the claimed peptide extension sequence; the extension sequence may be replaced with an entirely different

sequence and therefore the claim is indefinite. Therefore, there is insufficient basis in the independent claim for the limitation of the encoded peptide extension of claim 53 because the peptide extension of claim 53 may be *any* sequence that satisfies the charge restrictions. The dependent claims embrace embodiments that are not within the scope of the independent claims.

The same reasoning applies to independent claim 90 and dependent claims 91 and 95-98.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53, 63, 87-98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that claims 53 has been amended to include an expression vector optimized for use in a prokaryotic cell with peptide extension sequence comprising the carboxyl-terminal 57 amino-acid residues of a T7 gene 10B protein wherein under physiological conditions expression of the vector yields a fusion protein consisting essentially of the encoded peptide extension fused to the carboxy-terminus of the protein of interest. Applicants argue that the amendments bring claim 53 in

compliance with the written description requirement, although Applicant does not identify specific portions of the disclosure in support of this argument. The Office finds literal support for this amendment to claim 53 is provided in the specification, especially on p. 29, ¶ 3, to p. 30 and p. 31, ¶ 3 to p. 32.

The claims have been given broadest possible interpretation, wherein the terms "comprising" and "consisting essentially of" are interpreted as open ended, that is interpreted to mean that the invention claimed includes the recited sequence or elements *and* any conceivable sequence or element not specifically recited. Written description is, therefore, not provided for which peptide extension *comprises* the carboxy-terminal of a T7 gene 10B protein, which is to say the protein and *any other possible sequence without limits*. Further, sufficient written description is not provide for the limitation of the nucleic acid sequences *consisting essentially of* the encoded peptide fused to the carboxy-terminus of the protein of interest, which is to say the peptide fused to the terminus of the protein of interest *any and every other possible sequence without limits.* The open claim language common to independent claims 53, 90 and 93 place the claims beyond the scope of the disclosure. Therefore, all independent and dependent claims are rejected as failing to comply with the written description requirement.

Applicants' argument that the vector is optimized for use in all prokaryotic cells under physiological conditions is deemed not persuasive. A person of skill in the art would more likely conclude that the vector is optimized for use in certain bacterial cells, not all protozoans. For example, no information is provided regarding the claimed

invention for use in extreme halophilies of archaea, in which cytoplasmic proteins are typically very acidic, and require abundant positive charge provided by potassium ions for stability. It is uncertain whether the claimed peptide extensions would enhance or even affect protein solubility and folding in when expressed in such organisms.

Claims 53, 63, 64, 87-98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The previous rejection of the claims for lack of enablement based on the Wands factors is of record and reasoning therein applies herein with respect to sequences vectors comprising sequences and encoding substitutions.

Applicants argue persuasively that the disclosure is enabling for a nucleic acid encoding the 57 amino acid residue T7B peptide linked to the carboxy terminal of a protein of interest under physiological conditions and enhancing the protein's solubility and proper folding in *E. coli*. However, the disclosure does not reasonably provide enablement for which peptide extension *comprises* the carboxy-terminal of a T7 gene 10B protein, which is to say the protein and *any other possible sequence within the net negative charge boundary*. Further, information is not provided for the limitation of the nucleic acid sequences *consisting essentially of* the encoded peptide fused to the carboxy-terminus of the protein of interest. As "consisting essentially of" may be broadly

interpreted to mean the encoded peptide fused to the protein of interest plus any conceivable possible sequence, then the peptide fusion may include the T7B peptide, the protein of interest *any other possible sequence without limitation.* Thus, the claimed inventions are exceedingly broad and not enabled by the disclosure.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Response to Applicants' amendments and arguments

Claims 54-60 have been cancelled rendering all rejections under *35 USC § 102* to these claims moot

Claims 53, 63, 88, 89, 90, 91, 94, 95 and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by Rechsteiner et al. (US 5,366,871; see whole document; hereinafter the '871 patent).

This rejection is of record and briefly summarized herein below.

The claims are drawn to an expression vector encoding a fusion protein comprising a peptide extension and a protein of interest. The '871 patent teaches an expression vector to use in a cell where a peptide extension is linked to a gene of interest (e.g. Abstract; Fig 1). More particularly, the vector is an M13 vector encoding a fusion protein of an ubiquitin peptide extension in frame with a protein of interest – cRAS. (e.g. Fig. 1; col. 8, Example 1). Expression is observed in prokaryotes (e.g. col. 9, Example 2). The vector contains a polylinker or multiple cloning site. (e.g. col. 8, l. 55). Furthermore, the ubiquitin peptide extension contains the amino acid residues Ser-

Glu-Glu-Glu-Glu, which would necessarily have a net negative charge of –4, as it contains four acidic or negative side chains. Moreover, it is an intrinsic property of peptides in solution that if the pH ranges in solution is altered (e.g. by adding buffer to a solution) that the net charge for the peptide is changed (e.g. more or less negative). In addition, the fusion construct comprises additional peptide extensions consisting of the amino acid sequence, Pro-Gly-Cys-Met-Ser-Cys-Lys-Cys-Val-Leu-Ser (e.g. col. 8, Example 1), as well as multiple other peptide extensions as represented by SEQ ID NOs: 1-9, each of which would inhere a different net negative charge.

Applicants argue persuasively that the '871 patent does not teach a vector optimized for use in eukaryotic cells. Applicants also argue that there is no sequence similarity between the T7 gene 10B peptide extension of the instant application and the peptide extension described in Rechsteiner et al. However, as described under section 35 U.S.C. 112 above, due to language in the dependent claims wherein amino acids in the claimed sequence may be substituted or deleted to any other sequence, the instant claims reciting sequence encoding T7 gene 10B with amino acid substitutions or deletions may be interpreted to as being drawn to any possible sequence equal in length or shorter than the T7 gene 10B peptide. Therefore, the structure and sequence of the peptide extensions of the '871 patent are species of the genus of peptide extensions of the instant application.

With respect to functional characteristics and the nature of the product of interest, Applicants argue that the '871 patent does not teach that the peptide extensions therein would enhance the solubility or folding of the '871 protein of interest, which is ubiquitin.

In addition, Applicants note that ubiquitin was chosen because as the product of interest because it is a soluble protein. The Office notes that enhancement of solubility or folding in many instances may be subtle, simple addition of charged or hydrophilic amino acids to a polypeptide may enhance solubility. In addition, the Office asserts that instant claims are not limited to insoluble protein as proteins of interest; indeed the protein of interest is not limited in any way in the instant application so whether or not the Rechsteiner et al. protein of interest is soluble is of little moment.

Therefore, claims 53, 63, 88, 89, 90, 91, 94, 95 and 96 are rejected as being anticipated by Rechsteiner et al., US 5,366,871.

Conclusion

No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Guy Guidry, Ph.D. whose telephone number is 571-272-7928. The examiner can normally be reached on Monday through Friday 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Guy Guidry, Ph.D.

Examiner

Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER